species in the Old World, no less than the general hygienic and biological interest associated with the problem, make it important to study the situation promptly and in such fashion as to secure exact information on the various aspects of the question.

The American parasite in man may be identical with the European species, but, if not, two very similar species are now found side by side in certain regions. At least one of them affects man and either one or both of them also occur in other hosts in these regions. On the abundance and distribution of the parasites in other hosts as well as in man depends the frequency of human cases.

The life cycle of the tapeworms in this country must be precisely determined, whether a new species is involved or not, since this life cycle need not necessarily be identical with that reported for Europe. Evidently on the exact history of its varied relations to seasons and hosts depends both the manner and facility with which man is infected, and per contra the methods by which such infection may be regulated. In this connection it is essential to consider not only the last larval host but also the earlier phases of the life cycle as well. This is especially important since the species (*Cyclops leuckarti*) which in Europe serves as the first larval host is either rare or wanting on this continent.

Nickerson first showed that the source of human infection could be traced to a definite lake and Magath later demonstrated the occurrence of infected fish and thus of necessity infected intermediate hosts in a lake in the same general region. It is important to confirm these observations and to extend them to other waters for the purpose of determining the range and frequency of the parasite as well as the number and degree of infection of the intermediate hosts. Field studies are essential in securing the facts in the case and thus in furnishing a safe basis for views as to the probable future history of the parasite and possible means for its control and ultimate eradication.

With the purpose of studying the problem on the ground a field party has been organized and will carry on work this summer in northern Minnesota where the parasite has been so frequently reported. This party is directly in charge of the writer. Dr. T. B. Magath, of Rochester, Minn., will collaborate in the investigation and have control of the clinical experiments in particular. Dr. H. E. Essex of the University of Illinois will study the early development of the parasite and carry on the experiments in the field. Helpers will be secured as needed. The U. S. Bureau of Fisheries has undertaken to cooperate by sending an apprentice fish culturist to collect fish and maintain the aquaria. The Mayo Foundation has made a substantial contribution to the enterprise by furnishing reagents, apparatus and other help.

The problem will be attacked at once from several different angles. One line of work involves securing eggs of the adult tapeworm, developing them in cultures and employing them in feeding experiments to determine the species of crustacea or other small aquatic organisms which can function as first intermediate hosts. It may also be possible to collect naturally infected crustacea. The second stage in the life history will be sought by feeding such infected crustacea to small fish. While the time may not suffice to allow of full development in such first intermediate hosts, undoubtedly the plerocercoid larvae can be obtained as they have been previously from various fish, large and small. Among such specimens some will probably be sufficiently advanced in development to use in experiments with final hosts. In any event such material when carefully preserved and studied may show characters adequate to differentiate the plerocercoids of one bothriocephaloid tapeworm from those of another species. Here again the conclusions can be tested by feeding experiments with various hosts.

The problem can hardly be completely solved in a single summer, even with the varied attack planned. But preserved specimens will afford opportunity for continuing the study in my laboratory during the winter. Efforts will also be made to secure and transport living material so that feeding experiments can be continued there.

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SPECIAL ARTICLES

THE TOXICOLOGY OF CARBON MONOXIDE

THE toxicology of carbon monoxide gas always raises the mooted question as to whether carbon monoxide is poisonous *per se* or produces all its toxic effects from interference with proper oxygenation of tissues. In all higher animals it has been the general opinion of most pharmacologists that carbon monoxide is poisonous by virtue of its combining with hemoglobin to form CO hemoglobin and thus preventing the hemoglobin from combining with oxygen. The affinity of carbon monoxide for hemoglobin has been found to be some two hundred times greater than its affinity for oxygen. Carbon monoxide gas of itself is commonly regarded as being physiologically inert. Some recent work however seems to indicate that carbon monoxide is not as innocuous *per se* as it has been supposed to be. Thus Warburg (*Biochem. Zeit.*, 177, pp. 471, 1926) has shown that carbon monoxide may act as a poison in the absence of hemoglobin. He observed that carbon monoxide depresses the rate of oxygen consumption by yeasts and that the amount of carbon monoxide required to produce a given effect increased with a partial pressure of oxygen. Again, Haldane in a recent note (*Nature,* March 5, 1927, page 352) extended these observations to two higher organisms, wax moths, *Galleria mellonella* and the cress plant *Lepidium sativum.* He found that the moths behaved normally in as little as 2 per cent. of oxygen at atmospheric pressure, provided this gas is diluted with nitrogen. When however the oxygen is diluted with carbon monoxide about 16 per cent. of oxygen is needed for normal behavior. With smaller amounts of oxygen carbon monoxide is poisonous. Haldane also found that cress seeds do not germinate in an atmosphere of oxygen containing a certain amount of carbon monoxide.

In connection with the above observations the author wishes to call attention to certain observations which he has made and concerning which a brief note was published already (Macht, Blackman and Swigart, *Proc. of Exp. Bio. and Med.,* 1924, Vol. 91, pp. 227). While engaged in the study of the effects of various drugs and toxins on the growth of the seedlings of *Lupinus albus* studies were made on the growth of such seedlings in weak solutions of blood and hemoglobin. The procedure briefly consisted in growing seedlings of *Lupinus albus* in upright test tubes containing equal parts of distilled water and a plant physiological solution (Shive) on the one hand, and of other seedlings of *Lupinus albus* in exactly the same control solution plus small amounts of unknown substances to be studied. The elongation of the straight and well-defined roots was measured accurately in each case. It was found that 1 per cent. solutions of blood give a growth index as compared with a growth in normal nutrient solution without blood of about 72 per cent. Having studied repeatedly the effect of normal blood and normal hemoglobin solutions on the growth of *Lupinus albus* seedlings in the dark, experiments were made on the growth of the seedlings in solutions of blood containing various amounts of carbon monoxide hemoglobin. Here a new and unexpected observation was made. It was found the solution of carbon monoxide hemoglobin produced a poisonous effect on the seedlings as shown by an inhibition of their growth. The following four protocols will serve as illustrations.

EXPERIMENT NOVEMBER 3, 1925

Defibrated blood of a pig was saturated with pure carbon monoxide obtained by the addition of concentrated sulphuric acid to formic acid. A 1 per cent. solution of the normal pig's blood was made in Shive solution as described above; another 1 per cent. solution was made of the blood which was saturated with carbon monoxide. A third solution was made containing 0.5 per cent. of the monoxide blood. Ten seedlings each of *Lupinus albus* were carefully measured and immersed in each of the above solutions and all of the plants were left in the dark at a temperature of 22° C. After eighteen hours it was found that the growth of the seedlings in normal blood gave an index of 75 per cent. Growth in 1 per cent. carbon monoxide blood gave an index of 37 per cent. Growth in 0.5 per cent. of carbon monoxide blood gave an index of 48 per cent.

EXPERIMENT OCTOBER 9, 1925

Specimen of blood was obtained from a normal rabbit and a 1 per cent. solution was made. The rabbit was then allowed to inhale pure carbon monoxide until first signs of intoxication appeared. Blood was then drawn and it was found to contain about 30 per cent. of carbon monoxide hemoglobin. The growth of seedlings in a normal blood solution, and the blood obtained after inhaling carbon monoxide gave the following figures: Growth in normal blood 1 per cent. gave index of 72 per cent. Growth in carbon monoxide blood 1 per cent. gave index of 60 per cent.

EXPERIMENT MARCH 31, 1927

A rat was killed with carbon monoxide gas. The relative indices of growth in 1 per cent. of normal rat blood and 1 per cent. of blood from the poisoned animal were as follows: Normal 75 per cent., carbon monoxide blood 47 per cent.

EXPERIMENT APRIL 6, 1927

Pigeon was allowed to inhale carbon monoxide until convulsions occurred. Growth in solution of 1 per cent. of its blood was compared with growth in a 1 per cent. solution of normal pigeon's blood. The following results were obtained: Growth in normal blood 70 per cent., growth in carbon monoxide blood 50 per cent.

Similar experiments were performed with bloods of men and several other animals. In each case it was found that the growth of *Lupinus albus* seedlings was markedly inhibited by solutions of carbon monoxide blood and also solutions of pure carbon monoxide hemoglobin. It was found that in cases of very sensitive preparations a definite inhibition in growth of seedlings could be noted in solutions of monoxide blood diluted to 0.01 per cent. when the preparations were kept in the *dark* and at a temperature of 20° C. The above observations speak in favor of poisonous effects produced by carbon monoxide or rather carbon monoxide hemoglobin apart from an interference with oxygenation processes.

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